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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,637	08/10/2006	Giuseppe Giannini	2818-253	9505

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	
MAIL DATE	**DELIVERY MODE**
11/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,637	GIANNINI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. According to a preliminary amendment filed on Jan. 13, 2006, the applicants have amended claims 5, 7 and 9-11.

2. Claims 1-14 are pending in the application.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: It does not have signature of inventor, Maria Omella and furthermore, the date of signature is missing for the inventor, Frank Zunino.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

The instant compounds of formula (I) disclosed in claim 1 as well as in the specification on page 3 represent dihydro-camptothecins. However, all the examples given or prepared as well as methods of preparation are directed to preparing non-hydrogenated camptothecins. There is no teaching in the specification for preparing or using instant dihydro-camptothecins. There are no working examples present showing preparation of such compounds. There is no teaching either in the specification or prior art regarding existence of such dihydro-camptothecins. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the value of variable R and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to prepare such compounds and furthermore, to demonstrate their efficacy in vitro or in vivo models of every known cancer, viral disease or parasitic disease.

In regard to enablement rejection of instant claims 12-14 for using instant compounds for every known cancer, parasitic disease or viral disease, the specification teaches cytotoxic activity of non-hydrogenated camptothecins in vitro using lung cancer cells,

gastric carcinoma and Saccharomyces cerevisiae yeast (see pages 13-17 of specification). However, there is no teaching or guidance regarding cytotoxic activity of instant dihydro-camptothecins in any cell line. There are no working examples present showing efficacy of instant dihydro-camptothecins in any cell line. There is no teaching either in the specification or prior art regarding well known utility of dihydro-camptothecins in any type of cancer, viral disease or parasitic disease. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the value of variable R and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate their efficacy in vitro or in vivo models of every known cancer, viral disease or parasitic disease.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claim 1, the value of variable n8 is defined. However, this variable is not present in compounds of formula (I).

Regarding claim 1 for the value of variable Ar, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 6 recites the limitation "non-hydrogenated camptothecins" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 recites the limitation "non-hydrogenated homocamptothecins" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 does not end with a period.

Claims 10-14 provide for the use of compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 10-14 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

10. The following art rejections as well as ODP rejections are based on the assumption that the instant compounds are actually directed to non-hydrogenated camptothecins based on the examples in the specification.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6 and 9-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Dallavalle (J. Med. Chem. , cited on applicant's form 1449).

Dallavalle discloses Novel 7-oxyiminomethyl derivatives of camptothecin with potent in vitro and in vivo antitumor activity. The compounds 5-11, 13-16 and 19-44 (see table 1 on page 3265) anticipate the instant claims when m represents 0 in the instant compounds of formula (I).

12. Claims 1-6 and 9-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Penco (U.S. Patent 6,242,457).

Penco discloses Camptothecin derivatives having antitumor activity. The compounds disclosed in columns 7-9 by penco anticipate the instant claims when m represents 0 in the instant compounds of formula (I).

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1-4 and 7-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Marzi (WO 03/101995, cited on applicant's form 1449).

Marzi discloses Camptothecins with a modified lactone ring having antitumor activity. The compounds disclosed on pages 8 and 9 as well as claims 1-5 and 12-18 by Marzi anticipate the instant claims when m represents 1 in the instant compounds of formula (I).

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-6 and 9-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 10-17 of U.S. Patent No. 6,242,457. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds claimed in the cited patent anticipate the instant claims when m represents 0 in the instant compounds of formula (I).

16. Claims 1-6 and 9-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,589,939. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds claimed in the cited patent anticipate the instant claims when m represents 0 in the instant compounds of formula (I).

17. Claims 1-6 and 9-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 13-17 of U.S. Patent No. 7,105,492. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds claimed in the cited patent anticipate the instant claims when m represents 0 in the instant compounds of formula (I).

18. Claims 1-6 and 9-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/596,016. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds claimed in the cited application where U is absent and one of X or Y represents H and the other is absent anticipate the instant claims when m represents 0 in the instant compounds of formula (I).
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 11/596,015. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of instant claims are encompassed by the compounds claimed in the cited application. This is a provisional

obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/596,189. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds claimed in the cited application where U is absent and one of X or Y represents H and the other is absent anticipate the instant compounds of formula (I).

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

C. S. Aulakh

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Art Unit 1625